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Original Article

Pulmonary Congestion by Conventional Chest Radiography: Relationship With Hemodynamics and Mortality in Patients With Severe Aortic Stenosis

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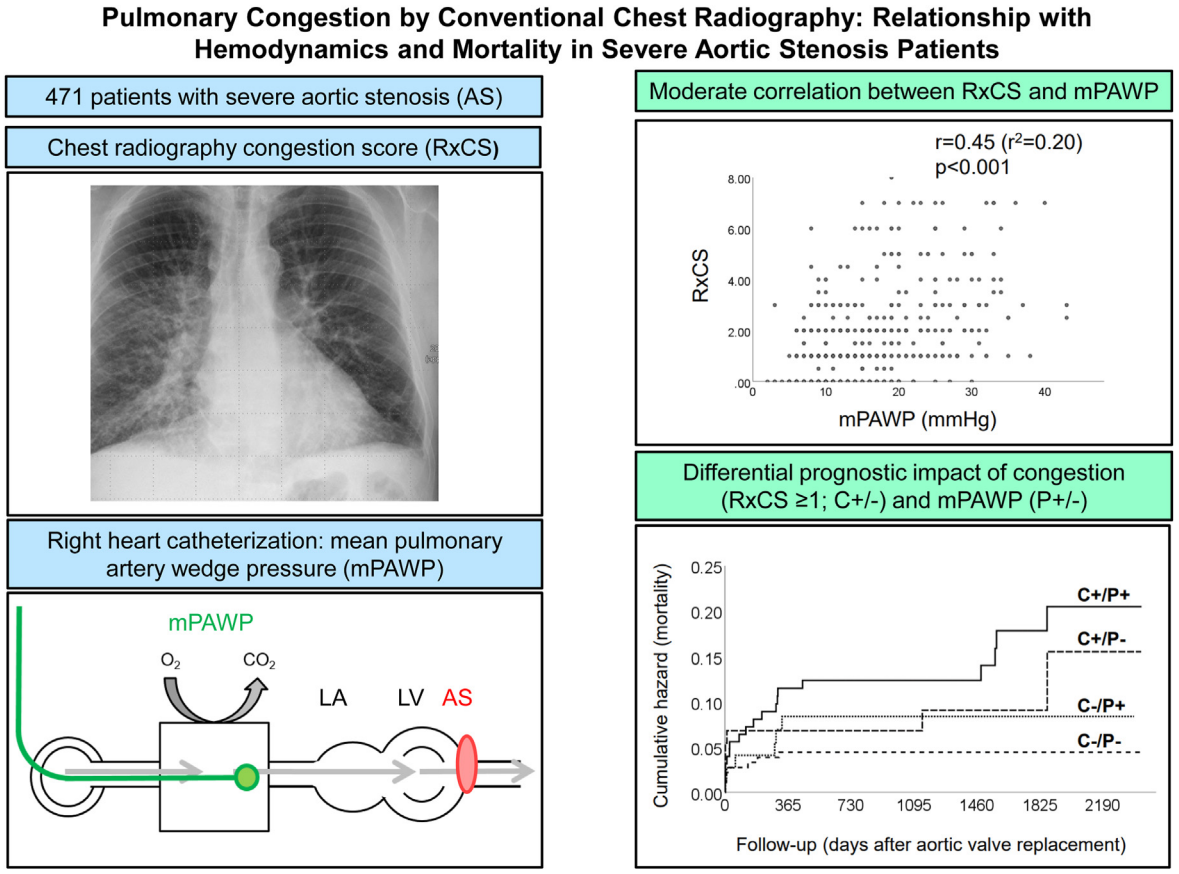

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ABSTRACT

Background: The relationship between chest radiograph (CXR) findings of pulmonary congestion and invasive hemodynamics and clinical outcomes in patients with cardiac diseases is unclear. We assessed the correlation between a CXR-based congestion score (RxCS) and the mean pulmonary artery wedge pressure (mPAWP) and the prognostic impact of RxCS and mPAWP in severe aortic stenosis (AS).

Methods: In 471 patients with severe AS undergoing right heart catheterization and upright CXR, the RxCS was calculated (6 items, maximum score: 10 points) independently by 2 radiologists (average value taken) blinded to clinical data. Congestion was defined as an RxCS $>$ 1. Four patterns were defined based on the presence or absence of congestion (C+ or C−) and elevated ($>$ 15 mm Hg) or normal mPAWP (P+ or P−).

Results: The median (interquartile range) RxCS was 1 (0-2). Patients with an RxCS $>$ 1 (n = 207) had a higher mean right atrial pressure, mean pulmonary artery pressure, mPAWP, and pulmonary vascular resistance than patients with an RxCS $\leq$ 1 (n = 264). However, the correlation between the RxCS and the mPAWP was moderate only (r = 0.45). Patients with a C+/P+ pattern had the worst hemodynamics, whereas C−/P− patients had the most favourable constellation. After a median post−valve replacement follow-up of 1361 days, mortality was higher in patients with RxCs $>$ 1 vs $\leq$ 1 as well as mPAWP $>$ 15 mm Hg vs $\leq$15 mm Hg. Mortality was highest in C+/P+ patients and lowest in C−/P− patients, whereas it was intermediate in C−/P+ and C+/P− patients.

Conclusions: In AS patients, RxCS and mPAWP have a significant but moderate correlation. Both RxCS and mPAWP provide prognostic information.

RÉSUMÉ

Contexte : Des zones floues persistent quant au lien entre les signes de congestion pulmonaire à la radiographie thoracique, les examens hémodynamiques invasifs et les résultats cliniques chez les patients atteints de maladies cardiaques. Nous avons donc évalué, d'une part, la corrélation entre le score radiologique de congestion pulmonaire et la pression capillaire pulmonaire moyenne et, d'autre part, la valeur pronostique du score radiologique de congestion pulmonaire et de la pression capillaire pulmonaire moyenne dans les cas de sténose aortique sévère.

Méthodologie : Chez 471 patients atteints d'une sténose aortique sévère soumis à un cathétérisme du cœur droit et à une radiographie thoracique en position debout, un score radiologique de congestion pulmonaire a été calculé (6 items, score maximal de 10 points) de façon indépendante par deux radiologistes (la valeur retenue étant la moyenne) qui ne connaissaient pas les données cliniques des patients. La congestion correspondait à un score radiologique de congestion pulmonaire $>$ 1. Quatre types ont été définis en fonction de la présence ou de l'absence de congestion (C+ ou C−) et d'une valeur de pression capillaire pulmonaire moyenne élevée ($>$15 mmHg) ou normale (P+ ou P−).

Résultats : La médiane (écart interquartile) du score radiologique de congestion a été de 1 (0-2). Les patients dont le score radiologique de congestion était $>$ 1 (n = 207) présentaient des valeurs moyennes plus élevées pour la pression auriculaire droite, la pression artérielle pulmonaire, la pression capillaire pulmonaire et la résistance vasculaire pulmonaire que les patients dont le score radiologique de congestion était $\leq$ 1 (n = 264). Cependant, la corrélation entre le score radiologique de congestion et la pression capillaire pulmonaire moyenne n'était que modérée (r = 0,45). Les patients de type C+/P+ avaient le profil hémodynamique le plus défavorable, tandis que les patients de type C−/P− avaient le profil le plus favorable. À l'issue d'un suivi médian de 1361 jours après un remplacement valvulaire, la mortalité était plus élevée chez les patients dont le score radiologique de congestion était $>$ 1 *vs* un score $\leq$ 1, de même que chez les patients dont la pression capillaire pulmonaire moyenne était $>$ 15 mmHg *vs* une valeur $\leq$ 15 mmHg. La mortalité la plus élevée a été observée chez les patients de type C+/P+, et la plus faible, chez les patients de type C−/P−, tandis qu'elle était intermédiaire chez les patients de types C−/P+ et C+/P−.

Conclusions : Chez les patients atteints d'une sténose aortique, on constate une corrélation significative mais modérée entre le score radiologique de congestion pulmonaire et la pression capillaire pulmonaire moyenne. Ces paramètres revêtent tous deux une valeur pronostique.

The conventional chest radiograph (CXR) has been used over many decades to describe cardiac anatomy and pathophysiology in numerous cardiac conditions.[1] However, other imaging modalities, such as echocardiography, computed tomography, and magnetic resonance imaging, currently provide more accurate information regarding cardiac anatomy and function. In current guidelines on the diagnosis and management of heart failure, the use of CXR is mentioned only briefly as a tool to confirm congestion and assess differential diagnoses,[2] and the current valve-disease guidelines do not mention CXR at all.[3] Still, in clinical practice, CXR is performed frequently to evaluate patients with possible cardiac diseases, and typically to assess hemodynamic status also. The prediction of "compensation" vs "decompensation" or "pulmonary venous hypertension," respectively, has a long tradition in classical radiology teaching. However, the accuracy of CXR for the diagnosis of heart failure has been found to be limited,[4] and the correlation between CXR findings and pulmonary artery wedge pressure (PAWP) has been reported

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See page 946 for disclosure information.

to be weak.[5] However, no larger invasive hemodynamic studies in this setting have been conducted, and the prognostic value of CXR features in patients with cardiovascular diseases is unknown. Experience from clinical practice also suggests that the spectrum of PAWP thresholds for the development of overt pulmonary congestion is broad.

In the present study, we systematically assessed the presence of pulmonary congestion by CXR in 471 patients with severe aortic stenosis (AS) who underwent right heart catheterization prior to aortic valve replacement (AVR). The aim of the study was to determine the relationship between pulmonary congestion and PAWP, and the long-term prognostic impact of pulmonary congestion and PAWP.

Methods

Study population

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. The study was approved by the local ethics committee, and a waiver of consent was granted. This is a retrospective analysis of systematically collected data on cardiac catheterization in patients with severe AS undergoing a highly standardized evaluation process prior to AVR in a single centre between January 2011 and January 2016 (entire cohort: n = 503) with a post-AVR follow-up of several years.[6] For this analysis, we included 471 patients in whom an upright CXR had been obtained prior to cardiac catheterization (in the vast majority, on the day before), with the image quality judged as sufficient for analysis. All patients subsequently underwent surgical or transcatheter AVR. We have reported previously on other hemodynamic aspects in this population.[6-11]

CXR reading

All CXR images were digitally stored. For the purpose of the present study, images were reviewed retrospectively in a systematic manner by 2 radiologists who were blinded to all clinical data, including hemodynamics. A previously described radiologic congestion score (RxCS) was determined.[12] The scoring system is described in Supplemental Table S1. In brief, the system includes 6 items, including redistribution of lung vessels, enlarged cardiac silhouette and peribronchial cuffing (each scored with 0-1 points), pleural effusion and Kerley's lines (each scored with 0-2 points), and lung opacity (scored with 0-3 points). Thus, the maximal RxCS is 10 points. The 2 radiologists performed an independent CXR assessment, and the RxCS used for analysis was the average of the 2 ratings. Thus, half points were possible also; for example, the RxCS was 1.5 if one of the radiologists gave a score of 1 point, and the other radiologist gave a score of 2 points. In accordance with Shochat et al.,[12] pulmonary congestion was defined as an RxCS > 1.

Cardiac catheterization

Procedures were generally ($> 95\%$) performed in the morning, with patients in the fasting state and after withholding loop diuretics and renin-angiotensin system inhibitors. Patients underwent coronary angiography using 5- or 6-F catheters via the femoral or radial artery and right heart catheterization using 6-F Swan Ganz catheters (Merit Medical, South Jordan, UT) via the femoral or brachial access. The midthoracic level was used as the zero reference point. Right atrial pressure, right ventricular pressure, pulmonary artery pressure, and PAWP were measured. The wedge position was confirmed by fluoroscopy and waveform analysis. Measurements were obtained at end-expiration, the mean PAWP (mPAWP) was calculated over the entire cardiac cycle, and v waves were included to determine mPAWP. This practice leads to higher values, compared to those from measurement of the end-diastolic PAWP.[13] However, for the estimation of the impact of the left heart contribution to pulmonary pressures and calculation of pulmonary vascular resistance (PVR), respectively, the mPAWP is preferred.[14,15] In patients with atrial fibrillation, at least 5 cardiac cycles were used to assess pulmonary artery pressure and PAWP (sinus rhythm—usually 3 cycles). An elevated PAWP was defined as an mPAWP > 15 mm Hg. Cardiac output was assessed by the indirect Fick method based on blood gases, which were collected simultaneously and in duplicate from the arterial catheter and the pulmonary artery. After completion of right heart catheterization, a coronary or a pigtail catheter was advanced into the ascending aorta for measurement of systolic, diastolic, and mean aortic pressure. In approximately two-thirds of the population, the aortic valve was crossed with a stiff wire, and the left ventricular end-diastolic pressure was measured using a pigtail catheter within a few minutes after the right heart catheter measurements and before coronary angiography. All pressure readings were double-checked by the operator, by manual review of the pressure tracings before they were entered into the report, and used for hemodynamic calculations, respectively. The transpulmonary gradient was calculated as the mean pulmonary artery pressure (mPAP) minus the mPAWP; PVR was calculated as the transpulmonary gradient divided by the cardiac output; and pulmonary artery compliance was calculated as the stroke volume divided by the differences of systolic and diastolic pulmonary artery pressure, where stroke volume is cardiac output divided by heart rate.

Echocardiography

All patients had an echocardiogram prior to cardiac catheterization, as a basis for the referral. Echocardiograms were performed by experienced cardiologists, according to contemporary guidelines, but not according to a specific study protocol. The data were retrospectively obtained from the reports, and not all patients had complete data.

Follow-up

All patients underwent surgical (73%) or transcatheter (27%) AVR following a median interval of 21 days (range: 12-35) postcatheterization. Information on long-term follow-up was obtained by a research assistant, from patients, general practitioners, and hospital or practice cardiologists. The clinical endpoint was all-cause mortality.

Statistical analysis

Categorical data are presented as numbers and percentages, and continuous data are reported as mean $\pm$ standard deviation, or median (interquartile range), as appropriate. Clinical characteristics and echocardiographic and hemodynamic data

Table 1. Clinical characteristics of the entire study population and according a to chest radiograph congestion score (RxCS) > 1 vs ≤ 1

Characteristic	All (n = 471)	RxCS > 1 n = 207	RxCS ≤ 1 n = 264	*P*
Age, y	74 ± 10	76 ± 9	72 ± 10	< 0.001
Gender, male	273 (58)	115 (56)	158 (60)	0.35
Body mass index, kg/m^2	27.9 ± 5.2	28.7 ± 5.5	27.4 ± 4.8	0.007
eGFR, mL/min per 1.73 m^2	74 ± 30	71 ± 31	77 ± 29	0.04
Hemoglobin, g/L	135 ± 16	133 ± 19	138 ± 14	0.002
Diabetes	98 (21)	49 (24)	49 (19)	0.18
Stroke	27 (6)	16 (8)	11 (4)	0.10
Chronic obstructive lung disease	52 (11)	28 (14)	24 (9)	0.13
FEV1, % predicted	87 ± 20	82 ± 20	91 ± 19	< 0.001
Heart rhythm				< 0.001
Sinus rhythm	408 (87)	158 (77)	250 (95)	
Atrial fibrillation	46 (10)	40 (19)	6 (2)	
Pacemaker	17 (3)	9 (4)	8 (3)	
Heart rate, bpm	69 ± 13	71 ± 15	68 ± 11	0.02
Medication				
Oral anticoagulation	89 (19)	57 (28)	32 (12)	< 0.001
Aspirin	290 (62)	117 (57)	173 (66)	0.046
Loop diuretics	226 (48)	124 (60)	102 (39)	< 0.001
Betablocker	226 (48)	108 (52)	118 (45)	0.11
ACEI and/or ARB	260 (55)	110 (53)	150 (57)	0.43
Digoxin	28 (6)	22 (11)	6 (2)	< 0.001
Spironolactone	23 (5)	12 (6)	11 (4)	0.42
B-type natriuretic peptide, ng/L	183 (76–408)	331 (159–747)	113 (55–243)	< 0.001
Symptoms				
Dyspnea NYHA class				< 0.001
I	95 (20)	30 (15)	65 (25)	
II	230 (49)	92 (44)	138 (52)	
III	125 (27)	68 (33)	57 (21)	
IV	21 (4)	17 (8)	4 (2)	
Mode of AVR				< 0.001
Surgical	343 (73)	133 (64)	210 (80)	
Transcatheter	128 (27)	74 (36)	54 (20)	

Data are given as numbers (%), mean ± standard deviation, or median (interquartile range), unless otherwise indicated.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; AVR, aortic valve replacement; bpm, beats per minute; eGFR, estimated glomerular filtration rate; FEV1, forced expiratory volume within the first second; NYHA, New York Heart Association.

in patients with RxCS > 1 vs ≤ 1 were compared using unpaired *t* tests, Mann-Whitney *U* tests, or χ^2 tests, as appropriate. Correlations between RxCS and hemodynamic parameters were described by Spearman correlation coefficients. Survival rates of patients with RxCS > 1 vs ≤ 1, and mPAWP > 15 mm Hg vs ≤ 15 mm Hg were compared using Kaplan-Meier plots and log-rank tests. Comparisons of the 4 RxCS/mPAWP groups (see details later) were performed using analysis of variance, Kruskal-Wallis tests, and χ^2 tests, respectively. Univariate and multivariate Cox regression was applied to describe the time-dependent association between clinical, echocardiography, and hemodynamic variables of interest and mortality. A *P*-value < 0.05 was considered statistically significant. Analyses were performed using the SPSS statistical package, version 25.0 (SPSS, Chicago, IL).

Results

Study population

We studied 471 patients with a mean age of 74 ± 10 years (58% males). The mean indexed aortic valve area was 0.42 ± 0.12 cm^2/m^2, and the mean left ventricular ejection fraction (LVEF) was 58% ± 12%. The mean mPAWP was 16 ± 8 mm Hg; the minimum mPAWP was 2 mm Hg; the maximum mPAWP was 43 mm Hg; and 204 patients (43%) had an mPAWP > 15 mm Hg. Detailed clinical, echocardiographic, and hemodynamic characteristics of the entire study population are shown in Tables 1 and 2.

CXR findings

The median (interquartile range) interval between CXR and cardiac catheterization was 1 day (1-1). In 87 patients (18%), the interval was > 1 day. The median RxCS was 1 point (0-2); the minimal RxCS was 0 points; the maximal RxCS was 8 points; and 207 patients had an RxCS > 1. A detailed description of the results of the CXR analysis by the 2 radiologists is provided in Supplemental Table S2. Two examples are shown in Figure 1.

Comparison of clinical characteristics of patients with RxCS > 1 vs ≤ 1

Patients with an RxCS > 1 were older, had higher body mass index, and had lower estimated glomerular filtration rate, hemoglobin, and forced expiratory volume within the first second than those with RxCS ≤ 1. The prevalence of atrial fibrillation and heart rate were higher in patients with RxCS > 1, and these patients also were more symptomatic, had higher B-type natriuretic peptide plasma concentrations, and were more likely to take oral anticoagulants, loop diuretics, and digoxin, compared to patients with RxCS ≤ 1 (Table 1).

Table 2. Data from echocardiography and cardiac catheterization of the entire study population and according to a chest radiograph congestion score (RxCS) > 1 vs ≤ 1

Measure	All (n = 471)	RxCS > 1 (n = 207)	RxCS ≤ 1 (n = 264)	*P*
Echocardiography				
LV end-diastolic diameter, mm	48 ± 8	48 ± 8	47 ± 7	0.09
Indexed LV end-diastolic diameter, mm	26 ± 4	26 ± 4	26 ± 4	0.15
LV ejection fraction, %	58 ± 12	55 ± 13	60 ± 11	< 0.001
E/e' (n = 226)	16.8 ± 8.6	19.2 ± 9.7	15.0 ± 7.2	< 0.001
Left atrial area, cm^2 (n = 190)	25 ± 7	28 ± 8	23 ± 6	0.001
Indexed left atrial area, cm^2/m^2 (n = 190)	13.4 ± 3.8	14.8 ± 4.0	12.3 ± 3.2	< 0.001
Tricuspid annular plane systolic excursion, mm (n = 178)	21 ± 5	20 ± 5	22 ± 4	0.001
Estimated sPAP, mm Hg (n = 213)	39 ± 13	43 ± 14	36 ± 11	< 0.001
Mean aortic valve gradient, mm Hg	47 ± 17	47 ± 18	47 ± 17	0.69
Aortic valve area, cm^2	0.79 ± 0.24	0.79 ± 0.26	0.79 ± 0.22	0.99
Indexed aortic valve area, cm^2/m^2	0.42 ± 0.12	0.42 ± 0.13	0.42 ± 0.12	0.68
Mitral regurgitation				< 0.001
No	224 (47)	68 (33)	156 (59)	
Mild	201 (43)	105 (51)	96 (36)	
Moderate	36 (8)	24 (11)	12 (5)	
Severe	10 (2)	10 (5)	0	
Coronary artery disease				0.28
None	249 (53)	111 (54)	138 (52)	
1-vessel	80 (17)	28 (14)	52 (20)	
2-vessel	66 (14)	30 (14)	36 (14)	
3-vessel	76 (16)	38 (18)	38 (14)	
Invasive hemodynamics				
Mean right atrial pressure, mm Hg	7 ± 4	8 ± 4	6 ± 3	< 0.001
RV end-diastolic pressure, mm Hg	9 ± 4	10 ± 4	8 ± 3	< 0.001
sPAP, mm Hg	39 ± 15	46 ± 16	34 ± 10	< 0.001
dPAP, mm Hg	15 ± 7	18 ± 8	13 ± 6	< 0.001
mPAP, mm Hg	25 ± 10	30 ± 11	22 ± 7	< 0.001
mPAWP, mm Hg	16 ± 8	19 ± 8	13 ± 7	< 0.001
Transpulmonary gradient, mm Hg	9 ± 5	10 ± 5	8 ± 4	< 0.001
Pulmonary vascular resistance, Wood units	2.1 ± 1.2	2.5 ± 1.4	1.8 ± 1.0	< 0.001
Pulmonary artery compliance, mL/mm Hg	3.4 ± 1.8	2.7 ± 1.4	3.9 ± 2.0	< 0.001
LV end-diastolic pressure, mm Hg (n = 327)	21 ± 8	22 ± 8	20 ± 7	0.01
Systolic aortic pressure, mm Hg	145 ± 25	144 ± 26	146 ± 25	0.28
Diastolic aortic pressure, mm Hg	68 ± 12	68 ± 12	69 ± 11	0.28
Mean aortic pressure, mm Hg	99 ± 14	97 ± 14	100 ± 13	0.09
Arterial oxygen saturation, %	95 (94–97)	95 (93–96)	96 (94–97)	< 0.001
Mixed venous oxygen saturation, %	69 (64–72)	66 (61–70)	70 (67–73)	< 0.001
Cardiac output, L/min	4.7 ± 1.0	4.4 ± 0.9	4.9 ± 1.1	< 0.001
Cardiac index, L/min per m^2	2.5 ± 0.5	2.3 ± 0.5	2.6 ± 0.5	< 0.001
Stroke volume, mL	70 ± 19	66 ± 19	74 ± 19	< 0.001
Stroke volume index, mL/m^2	37 ± 10	35 ± 9	40 ± 9	< 0.001

Data are given as number (%), mean ± standard deviation, or median (interquartile range), unless otherwise indicated.

The n is included next to the variable when the data set is incomplete.

dPAP, diastolic pulmonary artery pressure; E/e', ratio of peak early diastolic transmitral flow velocity to peak early diastolic mitral annular velocity; LV, left ventricular; mPAP, mean pulmonary artery pressure; mPAWP, mean pulmonary artery wedge pressure; PV, right ventricular; RxCS, chest radiograph congestion score; sPAP, systolic pulmonary artery pressure.

Comparison of echocardiographic findings and invasive hemodynamics of patients with RxCS > 1 vs ≤ 1

Patients with an RxCS > 1 had AS severity, as expressed by the indexed aortic valve area, similar to that of patients with RxCS ≤ 1, but LVEF was lower, left atrial size was larger, and mitral regurgitation was more severe in patients with an RxCS > 1, compared to those with RxCS ≤ 1. In addition, patients with an RxCS > 1 had higher mean right atrial pressure, mPAP, mPAWP, and PVR, and had lower pulmonary artery compliance, cardiac index, and stroke volume index than did patients with an RxCS ≤ 1 (Table 2).

Correlation between RxCS and mPAWP

A statistically significant correlation was present between the RxCS and the mPAWP, although it was only moderate ($r = 0.45$; Fig. 2). The correlation between RxCS and mPAWP was not worse in patients with an interval between CXR and cardiac catheterization > 1 day, compared to the correlation in those with an interval ≤ 1 day ($r = 0.50$ vs $r = 0.42$; $P < 0.001$ for both). All items of the RxCS were significantly correlated with the mPAWP, and correlation coefficients were similar ($r = 0.25$-0.34). The correlation between RxCS and mPAP was similar ($r = 0.49$), whereas it

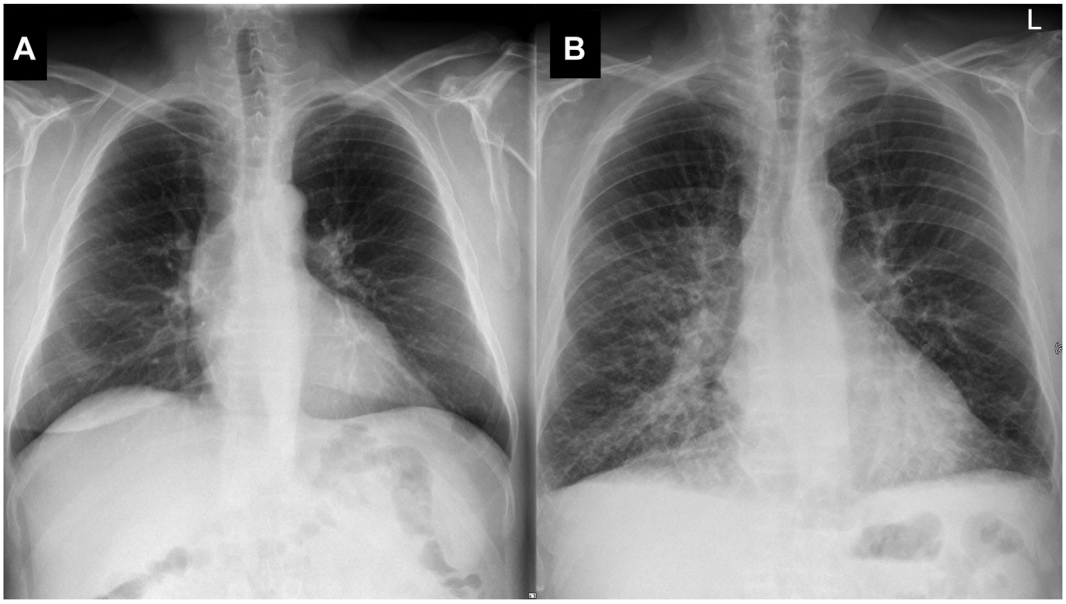

Figure 1. Two examples of a low and a high radiograph congestion score (RxCS; only posterior-anterior radiographs are shown). (**A**) A 51-year-old man. RxCS = 0; mean pulmonary artery pressure (mPAP) = 26 mm Hg; mean pulmonary artery wedge pressure (mPAWP) = 20 mm Hg; pulmonary vascular resistance (PVR) = 1.2 Wood units. (**B**) 79-year-old man. RxCS = 6; mPAP = 37 mm Hg; mPAWP = 18 mm Hg; PVR = 4.2 Wood units.

was weaker for other key hemodynamic parameters—PVR, $r = 0.36$; mean right atrial pressure, $r = 0.27$; left ventricular end-diastolic pressure, $r = 0.16$; and stroke volume index, $r = -0.31$. A significant correlation also was present between the RxCS and the ratio of peak early diastolic transmitral flow velocity to peak early diastolic mitral annular velocity (E/e'; $r = 0.38$; $P < 0.001$).

RxCS/mPAWP patterns

Given the limited correlation between RxCS and mPAWP, and the obvious presence of patients with "discordant" RxCS/mPAWP patterns (mPAWP > 15 mm Hg but RxCS ≤ 1, or vice versa), we defined 4 RxCS/mPAWP patterns, which depended on the presence or absence of congestion (C+ or C−; defined as RxCS > 1 or ≤ 1) and the presence or absence of mPAWP elevation (P+ or P−; defined as mPAWP > 15 mm Hg or ≤ 15 mm Hg). The number of patients with a C−/P−, C+/P−, C−/P+, and C+/P+ pattern, respectively, was 188 (40%), 79 (17%), 75 (16%), and 129 (27%).

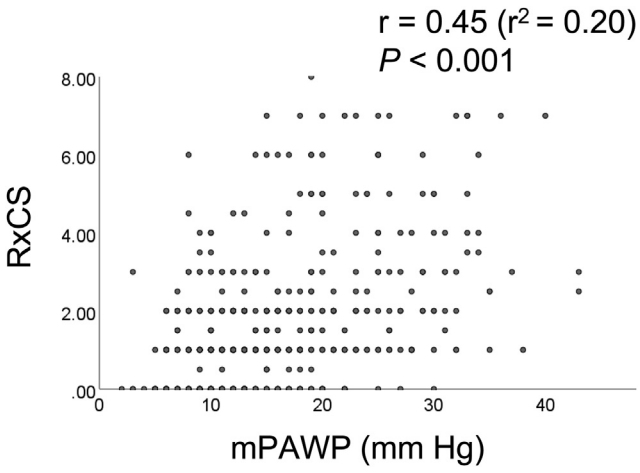

Figure 2. Scatterplot showing the correlation between the mean pulmonary artery wedge pressure (mPAWP) and the chest radiograph congestion score (RxCS). The Spearman correlation coefficient is shown.

Characteristics of patients with the 4 RxCS/mPAWP patterns

Patients with a C+/P+ pattern represented the oldest group, with the highest body mass index, the lowest hemoglobin, and the highest prevalence of atrial fibrillation (Supplemental Table S3). These patients were most symptomatic, had the highest B-type natriuretic peptide plasma concentrations, and were most likely to take oral anticoagulants, loop diuretics, spironolactone, and digoxin among all 4 of the groups. As shown in Supplemental Table S4, C+/P+ patients had the highest mean right atrial pressure, mPAWP, mPAP, and PVR, and they had the lowest LVEF, tricuspid annular plane systolic excursion, and stroke volume index. Conversely, C−/P− patients had the lowest mean right atrial pressure, mPAWP, mPAP, and PVR, and they had the highest LVEF, tricuspid annular plane systolic excursion, and stroke volume index among all 4 of the groups. Among the intermediate 2 groups, C−/P+ patients had higher mPAWP (by definition), mPAP, and mean right atrial pressure than C+/P− patients, but the PVR, LVEF, tricuspid annular plane systolic excursion, and stroke volume index were similar in C−/P+ and C+/P− patients.

Prognostic impact of RxCS and mPAWP

After a median follow-up of 1361 days (interquartile range: 957-1878) after AVR, 40 deaths (8%) had occurred. As shown in Figure 3, patients with an RxCS > 1 had a more than 2-fold mortality (hazard ratio 2.42) compared to that of

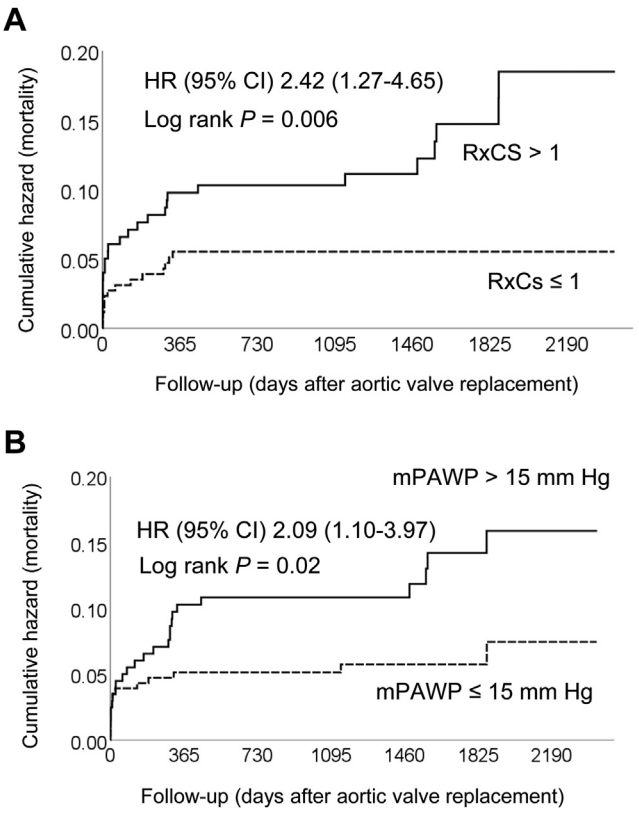

Figure 3. Kaplan-Meier plots showing cumulative events (mortality) for patients with a chest radiograph congestion score (RxCS) >1 vs ≤ 1 (Fig. 1A) and for patients with a mean pulmonary artery wedge pressure (mPAWP) >15 mm Hg vs ≤ 15 mm Hg (Fig. 1B). HR, hazard ratio; CI, confidence interval.

patients with an RxCS ≤ 1 (Fig. 3A). Similarly, patients with an mPAWP >15 mm Hg had a 2-fold higher mortality incidence (hazard ratio 2.09) than that of patients with an mPAWP ≤ 15 mm Hg (Fig. 3B). When used as continuous variables, both the RxCS {hazard ratio 1.18 [95% confidence interval (CI) 1.02-1.32]; $P = 0.03$ per score point increase} and the mPAWP [hazard ratio 1.05 (95% CI 1.01-1.08); $P = 0.01$ per 1 mm Hg increase] were significantly associated with mortality.

In Figure 4, mortality according to the 4 different RxCS/mPAWP patterns is shown: C+/P+ patients had the highest mortality, which was more than 3-fold higher than that for C−/P− patients (hazard ratio 3.43 [95% CI 1.50-7.85]; $P = 0.003$]. Patients with either a C+/P—or a C−/P+ pattern had intermediate mortality. The hazard ratio for C+/P—vs C−/P− was 2.21 (95% CI 0.80-6.09); $P = 0.13$; and the hazard ratio for C−/P+ vs C−/P− was 1.83 (95% CI 0.63-5.26); $P = 0.27$. However, in the multivariate analysis, the RxCS was not an independent predictor of mortality (Table 3).

Discussion

The present study, which systematically evaluated the association between CXR and invasive hemodynamics in 471 patients with severe AS, revealed several new findings. First, the RxCS—a simple tool to score the CXR—was statistically significantly associated with mPAWP and other key hemodynamic variables. Second, however, the correlation between mPAWP and RxCS was only moderate, and some patients had a high mPAWP but a normal RxCS, whereas other patients had an abnormal RxCS but a normal mPAWP. That is, both "concordant" and "discordant" patterns were seen. Third, patients with a C+/P+ pattern were the most symptomatic and had the worst hemodynamics, whereas C−/P− patients were least symptomatic and had the most-favourable hemodynamics. Finally, both mPAWP and RxCS were associated with mortality: C+/P+ patients had a >3-fold higher mortality than C−/P− patients, and patients with a discordant pattern (C+/P− or C−/P+) had intermediate prognosis.

Conventional CXR has been used for decades for the identification of pulmonary congestion.[1] However, no larger studies had been done to systematically validate CXR findings of "pulmonary venous hypertension" by right heart catheterization. The present study in a large cohort of patients with severe AS and a broad spectrum of hemodynamics confirms the presence of an association between the mPAWP and the RxCS and thereby underscores the relevance of the current teaching of CXR interpretation. We assume that the findings are applicable for not only AS patients but also patients with left heart disease in general. However, the association between mPAWP and RxCS was only moderate (only 20% of the variability of the RxCS was explained by the mPAWP), which can be interpreted in several ways. One could argue that the CXR is not accurate enough to detect pulmonary congestion, but this is probably not the appropriate interpretation. We have to take into account the methodology of our study, which used upright CXR (best suited for image interpretation) but right heart catheterization performed with the patient in the supine position. Body position affects hemodynamics, including mPAWP and mPAP. In a recent study, a difference of 1-2 mm Hg between supine and upright right heart catheterization was found.[16] In this study, however, "upright" was a 45° sitting position, and the majority of patients had precapillary pulmonary hypertension.[16] The differences might be larger for patients in the fully upright position and those with left heart pathologies. In addition, CXR and right heart catheterization were not performed simultaneously but with an intervening interval of approximately 1 day.

Apart from these methodological aspects, we have to consider that the relatively weak correlation between mPAWP and the presence and extent of pulmonary congestion is accurate and reflects normal human pathobiology. On one hand, the mPAWP threshold for the occurrence of pulmonary edema is likely to be highly variable. For the development of overt congestion, the chronicity of mPAWP elevation probably plays an important role when considering, for example, the different clinical presentation of acute vs chronic mitral regurgitation. On the other hand, the mPAWP seems not to be the only hemodynamic determinant of pulmonary congestion in left heart disease. As recently shown by Omote et al., in a seminal study on the pathophysiology of combined pre- and post-capillary pulmonary hypertension (mainly in the context of heart failure with preserved ejection fraction), right atrial pressure elevation with impaired lymphatic drainage may be relevant also.[17] In the present study, patients with abnormal RxCS had not only higher mPAWP than patients with normal RxCS but also higher mean right atrial pressure,

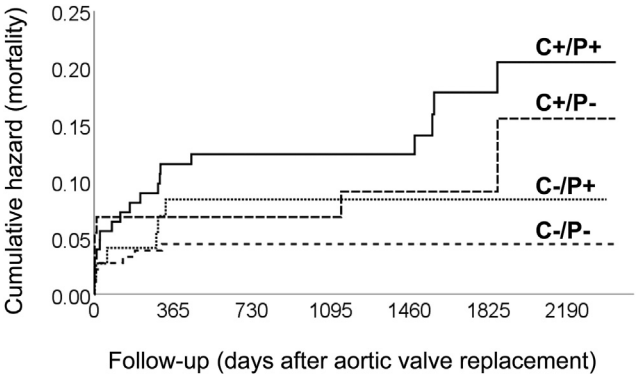

Figure 4. Kaplan plots showing cumulative events (mortality) for patients with different congestion (C) and pressure (P) patterns. Congestion was defined as a chest radiograph congestion score (RxCS) > 1; the cutoff for an elevated mean pulmonary artery wedge pressure was > 15 mm Hg. The 4 patterns were defined based on presence or absence of congestion (C+ or C−) and elevated or normal mean pulmonary artery wedge pressure (P+ or P−).

which could have contributed to the higher extent of congestion by impaired lymphatic drainage. Important to note is that the study by Omote et al. also showed that despite the traditional assumption that a high PVR protects from pulmonary edema, patients with combined pre- and post-capillary pulmonary hypertension (ie, elevated mPAWP and elevated PVR) had more severe pulmonary congestion (as assessed by ultrasound) than did patients with isolated post-capillary pulmonary hypertension (normal PVR).[17] In the present study, the RxCS also was associated with PVR, and the examples in Figure 1 highlight a substantial difference in the RxCS (higher in the patient shown in part **B**), despite a similar mPAWP, which may be explained by the significantly higher PVR in the patient shown in Figure 1B.

The extent of congestion was generally low (median RxCS of 1 point), a finding that was not unexpected, however, for a population of stable AS patients. The score used in our study had been developed in patients with acute myocardial infarction[12] and had not been evaluated in more stable patients, which represents a limitation of the study. In addition, a certain selection bias is likely in that only patients able to lay flat underwent cardiac catheterization. However, despite the overall relatively subtle signs of congestion, the RxCS emerged as a marker of long-term post-AVR mortality, although this finding was not statistically significant in the multivariate analysis. The prognostic value of the CXR as shown in our study underscores the clinical relevance of the CXR findings. An important point to note is that patients with a C+/P− pattern had a 2-fold higher mortality rate than C−/P− patients, which suggests that congestion is clinically important, even if it occurs at relatively low filling pressures (mPAWP in this group was only 11 mm Hg). On the other hand, patients with a C−/P+ pattern had a similar mortality rate as patients with a C+/P− pattern, indicating that hemodynamics are important even if a high mPAWP does not lead to apparent congestion. We have to acknowledge that the mortality data are hypothesis-generating only; as the number of patients was relatively small for an outcome study, the spectrum of RxCS values was relatively narrow, and the RxCS was not an independent predictor of mortality in the multivariate analysis.

The present data suggest that the value of CXR in patients with AS and other cardiovascular diseases has to be reconsidered. CXR is widely available and cheap and requires a very low radiation dose. Computed tomography and magnetic resonance imaging provide much more anatomic information than CXR, but in contrast to CXR, these examinations are performed with patients in the supine position and may therefore be less useful for the assessment of pulmonary congestion. Studies have looked at the ability of the computed tomography scan (routinely acquired for all transcatheter AVR candidates for the planning of the procedure) to predict the presence of pulmonary hypertension, mainly using the diameters of the pulmonary arteries. However, sensitivity of this method to predict pulmonary hypertension as assessed by right heart catheterization was generally poor.[18,19] Lung ultrasound has been reported to be more sensitive than CXR for the detection of pulmonary edema in patients with possible acute heart failure.[20] However, the specificity of lung ultrasound is limited,[1] and its role in more-chronic cardiac conditions is poorly defined.

Table 3. Univariate and multivariate Cox regression with mortality as the dependent variable

	Univariate		Multivariate	
Measure	HR (95%CI)	*P*	HR (95%CI)	*P*
Chronic obstructive pulmonary disease	3.02 (1.48−6.18)	0.02		
eGFR	0.86 (0.76−0.98) per 10 mL/min per 1.73 m^2	0.02		
Oral anticoagulation	2.73 (1.44−5.17)	0.002	2.08 (1.08-4.01)	0.03
Left ventricular ejection fraction	0.97 (0.95−0.99) per 1%	0.002		
Mitral regurgitation	2.15 (1.51−3.07) per grade	< 0.001	1.99 (1.38-2.87)	< 0.001
Coronary artery disease	1.34 (1.05−1.72) per number of affected vessels	0.02		
Mean arterial pressure	0.79 (0.62−0.99) per 10 mm Hg	0.047		
Mean right atrial pressure	1.10 (1.003−1.16) per 1 mm Hg	0.04		
Mean pulmonary artery pressure	1.04 (1.02−1.07) per 1 mm Hg	0.001		
Mean pulmonary artery wedge pressure	1.05 (1.01−1.08) per 1 mm Hg	0.01		
Pulmonary vascular resistance	1.34 (1.15−1.56) per 1 WU	< 0.001		
Pulmonary artery compliance	0.66 (0.50−0.85) per 1 mL/mm Hg	0.002		
RxCS	1.18 (1.02−1.32)	0.03		
C+/P+ vs C−/P−	3.43 (1.50−7.85)	0.03		

C+/P+, presence of congestion, elevated mean pulmonary artery wedge pressure; C−/P−, absence of congestion, normal mean pulmonary artery wedge pressure; CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; WU, wood unit.

Study limitations

The study has a number of limitations, as mentioned. They include the relatively small number of patients for a prognostic study, the interval of approximately 1 day between CXR and cardiac catheterization, the difference in patient body position between CRX and cardiac catheterization, and the relatively narrow spectrum of RxCS values. However, given the invasive nature of the study, the number of patients was still sizable, and to the best of our knowledge, similar data comparing CXR and invasive hemodynamics have not been available so far. In addition, the study was designed primarily as a cardiac catheterization study, and therefore, the incremental prognostic value of RxCS beyond that of E/e' cannot be determined from this study, as echocardiographic data were extracted from the clinical reports, if available, and a standardized protocol for the timing and acquisition of echocardiographic data was not employed.

Conclusions

The RxCS as a simple CXR-based score is significantly related to invasive hemodynamics in patients with severe AS. The relationship between mPAWP and pulmonary congestion is only moderately strong, however, and both parameters have prognostic implications in severe AS patients undergoing AVR. These data highlight the importance of CXR in not only patients with AS but also those with other left heart pathologies.

Ethics Statement

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

Patient Consent

The authors confirm that patient consent is not applicable to this article. The study was approved by the local ethics committee. A waiver of consent was granted.

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Disclosures

The authors have no conflicts of interest to disclose.

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Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2023.09.010.